

REMARKS

Claims 1, 8, 18, 23, and 26 have been amended. Claims 1, 8, 18, and 26 have been amended to insert the word “purified” before “polypeptide.” Support for this amendment can be found, for example, at page 42, lines 34-36, of the specification. Claims 1, 18, and 26 have been amended to delete reference to complementary sequences. Claims 18 and 23 have been amended to replace “15 base pairs” with “30 nucleotides.” Claim 26 has been amended to refer to “a sequence at least 100 nucleotides in length” rather than 20 nucleotides. Support for these amendments is found, e.g., at page 43, lines 35-39, of the specification. Claim 26 has also been amended to refer to “high stringency” conditions. Support for this amendment is found, e.g., at page 33, lines 20-21, of the specification. Claims 7 and 24 have been canceled. No new matter has been added. Upon entry of this amendment, claims 1, 6, 8, 15-18, 23, and 26, will be pending and under examination.

Objection to the specification

The Examiner objected to the specification for lacking patent numbers in the priority information on the first page. The specification has been amended to insert patent numbers corresponding to the priority applications that have issued.

Rejections under 35 U.S.C. § 101

Non-statutory subject matter

Claims 1 (e, f), 6, 7, 8 (g-l), 15-17, 18 (e, f), 23, 24, and 26 (e, f) were rejected as directed to non-statutory subject matter because the claimed polypeptides read on polypeptides found in nature. This rejection has been met by the amendment to claims 1, 8, 18, and 26 to specify that the polypeptides are purified. Withdrawal of this rejection is respectfully requested.

Utility

Claims 1 (e, f), 6, 7, 8 (g-l), 15-17, 18 (e, f), 23, 24, and 26 (e, f) were rejected as lacking patentable utility. According to the Examiner,

[t]he polypeptide encoded by a nucleic acid comprising the nucleotide sequence SEQ ID NO:3 lacks a specific utility. First, SEQ ID NO:3 encodes at least 3 different proteins, gag, pol, and env...The instant specification is silent as to the function and proteolytic breakdown of polypeptides encoded by SEQ ID NO:3, having at least 85% identity to SEQ ID NO:3, or having at least 15 or 20 nucleotides from SEQ ID NO:3. Indeed, no polypeptides or polypeptides sequences [sic] are taught in the specification.

Akiyoshi et al. (with inventor Jay Fishman); 1998; J. Virol. 72(5):4503-4507) teach a retrovirus having 99.9% identity to SEQ ID NO:3 (5 mismatches), and encoding the env protein (Fig. 1). Other encoded proteins are not disclosed therein. At page 4503, left col., para. 2, Akiyoshi et al. teach that Type C retroviruses from swine cell lines are known but no disease following infection has been identified.

Therefore, it can be concluded that the polypeptide(s) encoded by SEQ ID NO:3, having at least 85% identity to SEQ ID NO:3, or having at least 15 or 20 nucleotides from SEQ ID NO:3 do not have a specific utility.

The polypeptides have not been taught to have a substantial utility, or real world use...The specification does not assert any utility for the encoded polypeptides; thus, the polypeptides lack credible utility because no utility is offered.

This is traversed. The claims are drawn to various polypeptides, e.g., encoded by a nucleic acid molecule at least 85% identical to SEQ ID NO:1-3; to polypeptides encoded by specific sequences within SEQ ID NO:1-3; to polypeptides encoded by sequences at least 30 nucleotides in length selected from within SEQ ID NO:1-3; and to polypeptides encoded by a sequence at least 100 nucleotides in length that hybridizes under stringent conditions to a SEQ ID NO:3. The specification asserts specific, substantial, and credible utilities for the claimed polypeptides.

Swine are a potential source of organs for xenotransplantation (specification, page 1, lines 16-17). However, many phenomena associated with transplantation, such as immune suppression and viral coinfection, can promote activation of retroviral infection (specification, page 28, lines 17-19). Because swine carry endogenous retroviruses, it is important to recognize and manage retroviral infection and in swine and recipients of their organs. Accordingly, the specification teaches methods and reagents for detecting porcine retroviruses that are useful, e.g., for screening donor animals and xenografts recipients to determine infection and as a measure of

the appropriate level of immune suppression (specification, page 30, lines 25-27). The methods can include contacting a tissue sample with an antibody specific for a retroviral protein. See the specification, e.g., at page 24, lines 23-28. The specification also teaches ELISA-based assays for detecting the presence of porcine retroviral polypeptides. The ELISA assays include generation of porcine retroviral polypeptides and generation of antibodies specific for the polypeptides. See the specification, e.g., at page 39, lines 13-20. The Examiner's assertion that "no utility is offered" is incorrect.

The asserted utilities are specific because they are specific to the subject matter claimed. Not all retroviral proteins are useful in methods for detecting porcine retroviral sequences, e.g., in order to evaluate the risk of retroviral transmission by a xenograft or to detect a retroviral infection in a recipient of a swine xenograft. The asserted utilities are substantial, e.g., because they have real-world applicability to complications associated with xenotransplantation. Finally, the asserted utilities are credible. An assertion of utility is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. MPEP 2107.2.III.B. The logic underlying the assertion that the claimed polypeptides are useful, e.g., in detection of retroviral activation in the context of xenotransplantation is neither "seriously flawed" nor "based on facts inconsistent with that logic."

The Examiner argued that the claims lack utility, in part because the specification "is silent as to the function and proteolytic breakdown of polypeptides encoded by SEQ ID NO:3, having at least 85% identity to SEQ ID NO:3, or having at least 15 or 20 nucleotides from SEQ ID NO:3." The lack of details regarding proteolysis has no bearing on the determination of whether the claimed polypeptides are useful for the asserted utilities. The Examiner also argued that "no polypeptides or polypeptide sequences are taught in the specification." This is incorrect. The nucleotide sequence of SEQ ID NO:3 is disclosed in the specification and one of skill in the art can readily determine polypeptides encoded by SEQ ID NO:3. Furthermore, Figure 3 discloses polypeptide sequences.

The Examiner also argued that retroviruses such as human immunodeficiency virus and murine leukemia virus are associated with specific diseases. The Examiner stated that "Akiyoshi et al. teach that Type C retroviruses from swine cell lines are known but no disease following infection has been identified." Read in context, Akiyoshi et al. teaches that swine retroviruses indeed may present a risk of infection. The sentence cited by the Examiner and the passage preceding it read as follows:

The use of nonhuman species as sources of organs for human transplantation, i.e., xenotransplantation, is considered a potential solution to the shortage of human organs and tissues for transplantation. Advances in the biology of interspecies transplantation have enhanced the likelihood that clinical xenotransplantation will be performed in the near future (10, 14, 17, 37). A central concern regarding xenotransplantation is the risk of xenosis, infection by organisms transferred with the xenograft into both the transplant recipient and the general population (7, 13, 14). The risk of viral infection is increased in transplantation by the presence of factors commonly associated with viral activation, e.g., immune suppression, graft-versus-host disease, graft rejection, viral coinfection, and cytotoxic therapies (19, 28). Swine are among the most likely source species for xenografts for clinical use.

Type C retroviruses from cell lines of swine origin have been characterized (1, 2, 5, 6, 15, 23, 38-40, 43); as yet, no disease following infection by these viruses has been identified. A recent report demonstrated that a virus from PK15 (porcine kidney-derived) cells can infect human cells in vitro (31). (Akiyoshi et al., page 4503, left column, lines 1-20; emphasis added).

As the above-quoted passage indicates, xenotic transmission of pathogens is a central concern in xenotransplantation. This concern is supported by the demonstration that a porcine virus was found to infect human cells. The fact that endogenous retroviruses often do not exert pathogenic effects on their natural host has no bearing on the utility of the present claims.

Inoperability

The Examiner also stated that claims 1f, 7, 18 (e, f), 23, 24, and 26f are inoperative because the

claims are drawn to polypeptides encoded by complementary sequence to SEQ ID NO:3, or having at least 15 or 20 nucleotides from SEQ ID NO:3. DNA is comprised of a sense and antisense strand, also known as a coding and non-coding

strand of DNA with the antisense and non-coding strand art-recognized as the complementary strand. The complementary strand, then, does not encode any polypeptide. Thus, the complementary strand is inoperable in encoding a polypeptide.

This rejection has been met by the amendment of claims 1, 18, and 26, to delete reference to complementary sequences. Claims 7 and 24 have been canceled.

The Examiner also rejected claims 18, 23, and 24 for reciting "base pairs" because base pairs do not encode polypeptides. Claims 18 and 23 have been amended to refer to "nucleotides" instead of "base pairs." Claim 24 has been canceled.

Rejections under 35 U.S.C. § 112, first paragraph (enablement)

Claims 1 (e, f), 6, 7, 8 (g-l), 15-17, 18 (e, f), 23, 24, and 26 (e, f) were rejected.

According to the Examiner, "since the claimed invention is not supported by either a specific, substantial, credible, or operable asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention."

This rejection is traversed. As described in detail above, numerous utilities for the claimed polypeptides are asserted. One of skill in the art would know how to make and use the claimed polypeptides, e.g., in methods for detecting porcine retroviruses, in order to evaluate the risk of retroviral transmission by a xenograft or to detect a retroviral infection in a recipient of a swine xenograft. In view of the utilities of the polypeptides, withdrawal of this rejection is requested.

Rejections under 35 U.S.C. § 112, first paragraph (written description)

Claims 1 (e, f), 6, 7, 8 (g, l), 15-17, 18 (e, f), 23, 24, and 26 (e, f) were rejected as failing to comply with the written description requirement. The Examiner argued that "[t]he specification and claims do not set forth any structure or function for the claimed polypeptide encoded by SEQ ID NO:3, or having at least 15 or 20 nucleotides from SEQ ID NO:3. Also, this polypeptide is not in hand."

This rejection is traversed. The written description requirement must be applied in the context of the particular invention and the state of the knowledge. The claims are supported by the disclosure of SEQ ID NO:3, and by SEQ ID NO:1 and SEQ ID NO:2, which exhibit a very high degree of homology to SEQ ID NO:3. The determination of polypeptide sequences encoded by a given nucleotide sequence is well within the capabilities of a skilled artisan. Furthermore, various polypeptide sequences encoded by SEQ ID NO:3 are disclosed in Figure 3. Additional polypeptides that fall within the claims, e.g., polypeptides encoded by SEQ ID NO:2, are shown in Figure 2. There is simply no basis for the assertion that the specification lacks disclosure of structure of the claimed polypeptides. Applicant's disclosure of structures of representative species that fall within the claimed genera demonstrates possession of the claimed subject matter.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1 (e, f), 6, 7, 8 (g, l), 15-17, 18 (e, f), 23, 24, and 26 (e, f) were rejected as indefinite.

First, the Examiner said that “[t]he claims refer to ‘A polypeptide...’...retroviruses encode many polypeptides; therefore, it is not clear which polypeptide is being claimed.” Applicant disagrees that the claims are indefinite for this reason. Retroviral genomes do encode multiple polypeptides. The fact that a nucleotide sequence such as SEQ ID NO:3 encodes multiple polypeptides does not render claims to those polypeptides indefinite. As discussed above with respect to written description, identifying open reading frames in a DNA sequence is within the capabilities of one of ordinary skill. Breadth of a claim is not to be equated with indefiniteness.

Claim 1 was rejected for using the term “identical.” The Examiner stated that “one skilled in the art cannot know what a fraction of identical means.” This is traversed. This language is commonly used in the art to describe the degree of similarity between sequences. One of ordinary skill in the art understands the meaning of percent identity terms, in the context of sequence comparisons.

Claim 18f was rejected because “the term ‘homology’ is a qualitative term...Thus, one skilled in the art cannot know what 70% homology means. Additionally, it is not clear what a corresponding human, mouse, or primate retrovirus sequence is, or the last five 3’ bases may be.” This is traversed. The meaning of “homology” in this context is known in the art. Also, as explained in the specification at page 25, lines 23-33, “the percent of homology between two sequences is a function of the number of matching or homologous positions shared by the two sequences divided by the number of positions compared x 100.” (specification, page 25, lines 27-29). Regarding corresponding sequences, it is noted that retroviruses share a common genome organization (e.g., arranged so as to encode gag, pol, and env gene products, in that order). The common genome structure permits identification of corresponding regions in retroviruses of different species. Accordingly, the term “corresponding region” in claim 18 is clear.

Claims 1f, 7, 18 (e, f), 23, 24, and 26f were rejected for reciting polypeptides encoded by complementary strands of SEQ ID NO:3 or sequences at least 85% identical to SEQ ID NO:3. The amendment to the claims to delete reference to complementary sequences obviates this rejection.

Claim 18, 23, and 24 were rejected for referring to “base pairs.” This part of the rejection has been met by the amendment to claims 18 and 23 to refer to “nucleotides” rather than “base pairs.” Claim 24 has been canceled.

The Examiner rejected claim 26 because “the specification does not define the term ‘stringent conditions.’” This is traversed. The claim, as amended, refers to high stringency conditions. The specification provides that, “for definitions of high and low stringency see Current Protocols in Molecular Biology, John Wiley & Sons, New York, 1989, 6.3.1-6.3.6, hereby incorporated by reference.” (specification, page 42, lines 30-33). The specification also notes high stringency conditions at page 33, lines 20-21.

In view of the foregoing, Applicant requests withdrawal of the rejections of the claims under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 102(b)

Claims 18(e), 23, and 26(e) were rejected as anticipated by Hayashi et al., *J. Immunol.*, 149:1223-1229, 1992 (“Hayashi”). According to the Examiner, “Hayashi et al. teach AKV murine leukemia virus comprising Gly-Phe-Tyr-Val-Cys-Pro-Gly-Pro (amino acids 148-155 in Fig. 5), for example, encoded by nucleotides 325-348 of SEQ ID NO:3.”

Claim 18, as amended, is drawn to a polypeptide encoded by a sequence at least 30 nucleotides in length and selected from SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3, and further characterized by having less than 70% homology with the corresponding region in human, mouse and primate retroviral sequences, wherein the last five 3' bases are unique to the selected sequence. Hayashi does not anticipate this claim. The sequence disclosed in Hayashi is a murine retroviral sequence. Hayashi does not disclose any purified polypeptides encoded by a sequence at least 30 base pairs in length selected from SEQ ID NOs:1-3, and which has less than 70% homology with a corresponding region of a murine sequence because Hayashi discloses only murine sequences. Murine sequences necessarily have more than 70% homology with a murine sequence. Furthermore, the Hayashi’s Gly-Phe-Tyr-Val-Cys-Pro-Gly-Pro sequence is encoded by 24 nucleotides. The polypeptide of claim 18 is encoded by a sequence at least 30 nucleotides in length.

Claim 23 depends from claim 18 and specifies that the sequence is selected from SEQ ID NO:3. Claim 23 is not anticipated by Hayashi for the same reasons as discussed for claim 18.

Claim 26 is directed to a purified polypeptide encoded by a sequence at least 100 nucleotides in length that hybridizes under stringent conditions to a molecule selected from SEQ ID NO:1, SEQ ID NO:2, and SEQ ID NO:3. Hayashi does not disclose a purified polypeptide which has these features. Hayashi’s Gly-Phe-Tyr-Val-Cys-Pro-Gly-Pro sequence, cited by the Examiner as evidence of anticipation, is not a polypeptide encoded by a sequence at least 100 nucleotides in length.

For the foregoing reasons, Applicant requests that the Examiner withdraw the rejection of claims 18(e), 23, and 26(e) as anticipated by Hayashi.

Applicant : Jay A. Fishman
Serial No. : 10/723,552
Filed : November 26, 2003
Page : 16 of 16

Attorney's Docket No.: 14846-011004 / MGH 0978-2D

Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing attorney docket no. 14846-011004.

Respectfully submitted,

Date: 9/1/06

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (617) 542-8906


Laurie Butler Lawrence
Laurie Butler Lawrence
Reg. No. 46,593

21340313.doc